

## BIOGRAPHICAL SKETCH

NAME Jean X. Jiang		POSITION TITLE Ashbel Smith Professor		
EDUCATION/TRAINING				
INSTITUTION AND LOCATION		DEGREE	YEAR(s)	FIELD OF STUDY
Nanjing University		B.S.	1982-1986	Biochemistry
State University of New York at Stony Brook		Ph.D.	1987-1991	Biochemistry
Harvard Medical School		Post-doc	1991-1995	Cell Biology

### A. PERSONAL STATEMENT

The research areas in my laboratory are: **1)** Roles of connexins in suppression of bone cancer metastasis; **2)** Connexin channels in mechanotransduction and anti-oxidative stress of bone cells and tissues; **3)** Cell-cell communication and signaling in lens development and in prevention of cataract formation. I have extensive experience and strong interest and commitment in teaching and student training. I am the Associate Director for the Joint Biomedical Engineering Graduate Program of UTSA/UTHSCSA. I am currently involved in teaching four medical and graduate courses and serve as a course director for one of them. I served as a chair of the Graduate Admission Committee for the Biochemistry Program for three years and served as the Co-leader for the Membrane Biology and Cell Signaling Track in our Interdisciplinary Graduate Program for four years. Seventeen students have graduated from my laboratory with Ph.D. degrees. In addition, I have mentored 11 post-doctoral fellows, 39 graduate research rotation students, 5 summer undergraduate research fellows, 16 high school students, and six medical students. I have served as a faculty mentor for F30, F31 and K awardees and a K-awardees. Several of our trainees have won major awards, including a Young Investigator Award from American Society for Bone and Mineral Research, 2<sup>nd</sup> place in Texas High School Research Competition, 1<sup>st</sup> place in MD student research award for Xianya students, Greehey Graduate Fellowship in Children's Health, the Excellence in Women's Health Scholarship, Poster and travel Awards, etc.

### A. Positions and Honors.

#### Positions and Employment

08/1995 - 08/1997	Instructor, Department of Cell Biology, Harvard Medical School, Boston
09/1997 - 08/2003	Assistant Professor (tenure-track), Department of Biochemistry University of Texas Health Science Center at San Antonio
09/2003 - 08/2007	Associate Professor (tenured), Department of Biochemistry, University of Texas Health Science Center at San Antonio
09/2007 - Present	Professor (tenured), Department of Biochemistry, University of Texas Health Science Center at San Antonio
11/2016 – Present	Ashbel Smith Professor, Department of Biochemistry and Structural Biology, UT Health Science Center at San Antonio
09/2011-Present	External member, Wills Vision Research Center at Thomas Jefferson Univ
03/2012 – Present	Visiting Professor, Northwestern Polytechnical University, Xian, China
01/2015-01/2016	Interim Associate Director, Joint Biomedical Engineering Program of Univ of Texas at San Antonio/Univ of Texas Health Science Center at San Antonio
01/2016-present	Associate Director, Joint Biomedical Engineering Program of Univ of Texas at San Antonio and Univ of Texas Health Science Center at San Antonio

#### Other Experience and Professional Memberships

1999, 2003	Reviewer, National Science Foundation
2000	Member, review panel for research applications of American Cancer Society
2001-present	Reviewer, US Department of Veterans Affairs; Wellcome Trust, UK; Diabetes UK; Australia Research Foundation; State of Kansas; State of Louisiana; Pennsylvania State

	University; Czech Science Foundation; University of Auckland, New Zealand; European Research Council; French National Research Agency
2001, 2004-present	Ad hoc Member, NIH AED and BVS study sections
2013	Ad hoc Member, NIH ZRG1 study section
2005-2009	Regular Member, NIH AED study section
2016	Ad hoc Member, NIH SBSR study section
2001 – present	Managing editor, <i>Frontier in Biosciences</i>
2005, 2007	Guest Managing Editor, <i>Cell Communication and Adhesion</i>
2006-2011	Member, Editorial Board, <i>Journal of Biological Chemistry</i>
2009-2011	Member, Editorial Board, <i>Current Chemical Biology</i>
2009—present	Member, Senior Editorial Board, <i>International Journal of Biochemistry and Molecular Biology</i>
2011-present	Associate Editor, <i>BMC Cell Biology</i>
2012-present	Associate Editor, <i>Journal of Bone and Mineral Metabolism</i>
2013-2014	Members-at-Large Board Member, International Chinese Musculoskeletal Research Society (ICMRS)
2014-present	Member, Working Group on Strategic Global Partnerships, Association for Research in Vision and Ophthalmology (ARVO)
2015-2018	Member, Global Members Committee, Association for Research in Vision and Ophthalmology (ARVO)

### **Honors**

1992-1995	National Research Service Award (NRSA), NIH
2002	San Antonio's 40 under 40 Rising Star
2002	Junior Research Incentive Award, UTHSCSA
2003	Junior Research Incentive Award, UTHSCSA
2004	Junior Research Incentive Award, UTHSCSA
2012	University of Texas LEAD (Leadership) Fellow
2016	Cancer Therapy & Research Center (CTRC) Discovery of the Year Award
2016	Ashbel Smith Professorship by University of Texas Board of Regents

### **B. Selected peer-reviewed publications (in chronological order).** (Selected out of 106 publications)

1. **Jiang, J.X.**, and Goodenough, D.A. (1996). Heteromeric connexon formation in lens gap junctions. *Proc. Natl. Acad. Sci. USA* . 93, 1287-1291.
2. Gu, S., Roderick, H.L., Camacho, P., and **Jiang, J.X.** (2000). Identification and characterization of an amino acid transporter expressed differentially in liver. *Proc. Natl. Acad. Sci.* 97, 3230-3235.
3. Cherian, P.P., Siller-Jackson, A. J., Gu, S., Wang, X., Bonewald, L.F., Sprague, E. and **Jiang, J.X.** (2005). Hemichannels formed by connexin 43 provide a novel pathway for the release of prostaglandin E2 by osteocytes in response to mechanical strain. *Mol. Biol. Cell* 16, 3100-3106. (\*Highlighted as a hottest paper, *Science STKE* 291, tw242, 2005). PMCID: PMC1165395
4. Banks E.A., Yu, X.S, Qian, S. and **Jiang, J.X.** (2007). Promotion of lens epithelial-fiber differentiation by C-terminus of connexin 45.6, a role independent of gap junction communication *J Cell Sci.* 12, 3602-3612.
5. Siller-Jackson, A.J., Burra, S., Gu, S., Bonewald, L.F., Sprague, E., and **Jiang, J.X.** (2008) Adaptation of connexin 43-hemichannel prostaglandin release to mechanical loading *J. Biol. Chem.* 283, 26374-26382.
6. Banks, E.A., Toloue, M.M., Shi, Q., Zhou, Z.J., Liu, J., Nicholson, B.J. and **Jiang, J.X.** (2009) Connexin mutation that causes dominant congenital cataracts inhibits gap junctions, but not hemichannels, in a dominant negative manner. *J. Cell Sci.* 122: 378-388.
7. Xia, X., Batra, N., Shi, Q., Bonewald, L.F., Sprague, E., and **Jiang, J.X.** (2010) Prostaglandin promotion of osteocyte gap junction function through transcriptional regulation of connexin 43 by GSK-3- $\beta$ -catenin signaling. *Mol. Cell. Biol.* 30, 206-219. PMCID:2798309

8. Shi, Q., Banks, E.A., Yu, X.S., Gu, S., Lauer, J., Fields, G.B., and **Jiang, J.X.** (2010) An amino acid residue V362 plays a critical role in maintaining the structure of Connexin 50 C-terminus and in lens epithelial-fiber differentiation. *J. Biol. Chem.* 285, 18415-18422. PMID:2881767
9. Burra, S., Nicoletta, D.P., Francis, W.L., Freitas, C.J., Mueschke, N.J., Poole, C., and **Jiang, J.X.** (2010) Dendritic process of osteocytes is a mechanotransducer that induces the opening of hemichannels. *Proc. Natl. Acad. Sci.* 107, 13648-13653. PMID: 2922284
10. Liu, J., Xu, J., Gu, S., Nicholson, B.J., and **Jiang, J.X.** (2010) Aquaporin 0 regulates gap junction function via interaction with connexin 50 and cell adhesion function. *J. Cell Sci.* 124, 198-206. PMID: 3010190
11. Liu, J., Ek Vitroin, J.F., Weintraub, S.T., Gu, S., Shi, Q., Burt, J.M., Burt, J.M., and **Jiang, J.X.** (2011). Phosphorylation of connexin 50 by protein kinase A enhances gap junction and hemichannel function. *J. Biol. Chem.* 286:16914-28. PMID: 3089535
12. Shi, Q., Padmanabhan, R., Villegas, C.J., Gu, S., and **Jiang, J.X.** (2011) Membrane topological structure of SNAT4 neutral amino acid transporter. *J. Biol. Chem.* 286, 38086-38094. PMID:3207422
13. Batra, N., Burra, S., Siller-Jackson, A.J., Gu, S., Xia, X., Weber, G., DeSimone, D., Bonewald, L.F., Lafer, E.M., Sprague, E., Schwartz, M.A., and **Jiang, J.X.** (2012) Mechanical stress activates integrin  $\alpha 5 \beta 1$  induces opening of connexin 43 hemichannels. *Proc. Nat. Acad. Sci.* 109:3359-64. PMID:3295295 (*highlighted in "Editor's Choice", Science, 335, 1021 (2012)*).
14. Wang, K., Gu, S., Yin, X., Weintraub, S.T., Hua, Z. and **Jiang, J.X.** (2012) Developmental truncations of connexin 50 by caspases adaptively regulate gap junctions/hemichannels and protect cells against UV radiation. *J. Biol. Chem.* 287, 15786-15797. PMID: 22418432.
15. Kar, R., Riquelme, A., Werner, S., and **Jiang, J.X.** (2013) Connexin 43 channels protect osteocytes against oxidative stress-induced cell death. *J. Bone Miner. Res.* 28, 1611-1621. PMID3688648
16. Kar, R., Riquelme, M.A., Werner, S., and **Jiang, J.X.** (2013) Connexin 43 channels protect osteocytes against oxidative stress-induced cell death. *J. Bone Miner. Res.* 28, 1611-1621. PMID3688648
17. Batra, N., Riquelme, M.A., Burra, S., and **Jiang, J.X.** (2014) 14-3-3 $\theta$  facilitates plasma membrane delivery and function of mechanosensitive connexin 43 hemichannels. *J. Cell Sci.* 127, 137-146. PMID3874784
18. Lo, W-K., Biswas, S., Brako, L., Shiels, A., Gu, S., and **Jiang, J.X.** (2014) AQP0 targets interlocking domains to control integrity and transparency of eye lens. *Invest. Ophthalmol. Vis. Sci.* 55, 12021-1212.
19. Batra, N., Burra, S., and **Jiang, J.X.** (2014) Direct regulation of osteocytic connexin 43 hemichannels through AKT kinase activated by mechanical stimulation. *J. Biol. Chem.* 289, 10582-10591. PMID4036178
20. Xu, H., Gu, S., Riquelme, M.A., Burra, S., Callaway, D., Cheng, H., Guda, T., Schmitz, J., Fajardo, R., Werner, S.L., Zhao, H., Shang, P., Johnson, M.L., Bonewald, L.F., and **Jiang, J.X.** (2015) Connexin 43 channels are essential for normal bone structure and osteocyte viability. *J. Bone Miner. Res.* 30, 550-562
21. Zhou, J.Z., Riquelme, M.A., Ellies, L.G., Sun, L-Z., **Jiang, J.X.** (2015) Differential impact of adenosine nucleotides released by osteocytes on breast cancer growth and bone metastasis. *Oncogene* 34, 1831-1842.
22. Shi, Q., Gu, S., Yu, X.S., White, T.A., Banks, E.A., and **Jiang, J.X.** (2015) Connexin controls cell cycle exit and cell differentiation by directly promoting cytosolic localization and degradation of E3 ligase Skp2. *Dev. Cell.* 35, 483-496.
23. Zhou, J.Z., Riquelme, M.A., Gu, S., Kar, R., Gao, X., , Sun, L and **Jiang, J. X.** (2016) Osteocytic Connexin 43 hemichannels suppress breast cancer growth and bone metastasis. *Oncogene* 35, 5597-5607

## C. Research Support

### Ongoing Research Support

RO1 (EY012085) NIH/NEI "Intracellular Communication in the Eye lens" The major objective of this grant is to understand the roles of connexin 50 in maintaining lens transparency and homeostasis, and cell protective function against UV and oxidative stress. Role: PI	Jiang (PI)	09/01/2012-08/31/2017.
RO1 (CA196214) NIH/NCI "Connexin hemichannels in suppression of breast cancer bone metastasis" The major objective of this grant is to explore the mechanistic roles of activated Cx43 hemichannels in osteocytes in inhibition of breast cancer cell migration and bone metastasis and the involvement of purinergic signaling in cancer cells. Role: Contact PI.	Jiang and Sun (MPI)	02/01/2016-01/31/2021
NIH/NIA "CSF-1 gene expression in osteoclast biology" The major objective of this grant is to understand the roles of CSF-1 in osteoclast differentiation and maturation and its influence on other bone cells. Role: PI	Jiang (PI)	03/01/2017-3/31/2018
Research Grant Welch Foundation "Modulating hemichannel activities using targeting antibodies" The objective of this project is to characterize the biochemical/biophysical properties of the binding of monoclonal antibody targeting Cx43 hemichannels.	Jiang (PI)	06/01/2016-05/31/2019
Research grant President's Translational and Entrepreneurial Research Fund/UTHSCSA "Antibodies against Cx43 for Suppression of Breast Cancer Bone Metastasis" The objective of this project is to test the effects of hemichannel activating antibodies on suppression of breast cancer bone metastasis. Role: PI	Jiang (PI)	01/01/2017-08/31/2017
Research Grant Texas Prevention & Research Institute of Texas (CPRIT) "Inhibition of Breast Cancer Metastasis to the Bone by microRNA Transmission Through Gap Junctions" The objective of this project is to explore the role of gap junctions in transmitting miRNA to inhibit breast cancer bone metastasis. Role: Co-PI	Nicholson (PI)	06/01/2015-05/31/2017
R21(AR066925) NIH/NIAMS "Non-collagenous proteins vs bone fragility" The objective of this project is to establish the relationship between components of extra-fibrillar matrix and material properties of the bone. Role: Co-investigator	Wang (PI)	07/01/2014-06/30/2016 (Non-cost extension)
R21(AR065641) NIH/NIAMS "Intrafibrillar mineralization vs bone fragility" The objective of this project is to understand the underlying mechanism concerning the intrafibrillar mineralization and bone structure and strengths. Role: Co-Investigator	Wang (PI)	07/25/2014-06/30/2016 (Non-cost extension)

## **Completed Research Support**

Research Grant                      Jiang (PI)                      06/01/2013 - 05/31/2016  
Welch Foundation  
"Identification of sodium and glutamine binding site of SNAT using SCAM approach"  
The objective of this project is to identify ion and substrate binding sites of amino acid transporter SNAT1.  
Role: PI

Research grant                      Sayre (PI)                      01/01/2016-12/31/2016  
CBN/IIMS, UTHSCSA  
"Targeting astrocyte hemichannels to halt secondary spread of injury after spinal cord injury"  
The objective of this project is to test the effects of hemichannel blocking antibodies on recovery of spinal cord injury and protection of neuronal damages.  
Role: Co-PI

Pilot Grant                      Jiang (PI)                      01/01/2013-12/31/2014  
UTHSCSA-UTSA Center for Innovation in Drug Discovery Pilot Program  
"Identifying drug candidate(s) targeting on osteocytic connexin 43 hemichannels for treatment of cancer bone metastases"  
The object of this project is to use HTS and medicinal chemistry approaches to identify chemical reagents that inhibit bone cancer metastasis

## Research Plan

The major research areas in Jiang's laboratory focus on three major directions in **cancer, skeletal** and **eye** research.

### **Connexin channels and purinergic signaling in cancer bone metastasis**

Bone metastasis is a deadly complication occurring frequently in patients with advanced breast cancers. To date, most research has focused on metastasized cancer cells themselves or tumor-supporting functions of the bone microenvironment on metastasized cancer cells. We propose a new mechanism via connexin (Cx) 43 hemichannels, by which *we can augment intrinsic, anti-metastatic roles of bone cells*. The goal of this research is to establish the importance of osteocytic Cx43 hemichannels as a potential, novel drug target. We have three specific aims: 1). To test the hypothesis that active osteocytic Cx43 hemichannels inhibit breast cancer cell metastasis; 2). To test the hypothesis that osteocytic Cx43 hemichannels activated by mechanical loading play a critical role in the inhibition of breast cancer bone metastasis; 3) To test the hypothesis that the P2X7 receptor in breast cancer cells activated by ATP released by osteocytic Cx43 hemichannels is responsible for suppression of bone metastasis.

### **Connexin channels in eye lens homeostasis and protection against oxidative stress.**

Gap junction intercellular communication (GJIC) is essential for the survival and metabolic homeostasis of the lens. Mutations of connexin genes are leading causes of human congenital cataracts and gene deletion of lens connexins in mouse also results in cataract formation. We have three research aims: We will first determine the distinctive roles of gap junctions and hemichannels in the differentiating lens fibers. We will then determine the importance of protein kinase A (PKA) phosphorylation of Cx50 in the lens by examining the effect of PKA on the interactions between Cx50 and ZO-1 and then elucidate the distinctive function of Cx50 channels enhanced by PKA activation to promote lens transparency. Finally, we will determine the role of connexin truncation in mature lens fibers and their response to oxidative stress.

### **Gap junctions and hemichannels in transmitting mechanical signals and promoting bone formation**

Mechanical loading experienced by skeletal tissues plays an important role in bone formation and remodeling. The objective is to define the distinctive, mechanistic role of Cx43 hemichannels in mediating the anabolic effect of mechanical loading on the skeletal tissues. Three specific aims are proposed: 1) To test the hypothesis that osteocytic Cx43 hemichannels play a crucial role in mediating anabolic function of mechanical loading on skeletal tissue. 2) To test the hypothesis that osteocytic Cx43 hemichannels mediate anabolic function of mechanical loading via PGE2 signaling and sclerostin and bone remodeling molecule expression in osteocytes. 3) To test the hypothesis that activation and inactivation of Cx43 hemichannels are specifically regulated by integrin activation/cytoskeleton and cell signaling, respectively.

### **Translational Project**

We are in the process of developing new reagents targeting connexin channels for the potential treatment of breast cancer metastasis, spinal cord injury and osteoarthritis.